UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,482	04/03/2001	Menashi A. Cohenford	11.018011	2116

38732 7590 07/28/2005

CYTYC CORPORATION
250 CAMPUS DRIVE
MARLBOROUGH, MA 01752

EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 07/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/825,482	COHENFORD ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-54 and 57-96* is/are pending in the application.

4a) Of the above claim(s) *66,69,75,90 and 92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-54,57-65,67,68,70-74,76-89,91 and 93-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of SEQ ID NO: 6 and species election of HPV strain 16 in the reply filed on May 5, 2005 is acknowledged. Claims readable on the elected sequence and species are claims 50-54, 57-65, 67, 68, 70-74, 76-89, 91, and 93-96. Accordingly claims 66, 69, 75, 90 and 92 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1-49 and 55-56 have been canceled.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/9/2004 has been entered.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Note***No limiting definition for the terms "substantially complementary" and sufficiently complementary" have been provided in the specification or claims of the instant invention. Accordingly, the terms are being interpreted broadly by the Examiner as having some complementarity.

5. Claims 50-54, 57, 59-65, 67-68, 70-74, 76, 79-84, 86-89, 91, 93-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinman (US 5,849,497, December 15, 1998) and Orum et al (Nucleic Acids Research, vol. 21, no. 23, pages 5332-6, 1993) in view of Lancaster et al (US 5,863,717, January 26, 1999) and further in view of Bauer et al (US 5,639,871, June 1997). Regarding claims 50-52, 74, 79-80, 82-83 Steinman teach a PCR method of detection of selected strain of an organism, wherein said organism may be a pathogenic organism, said method comprising providing a sample that may comprise at least one selected and non-selected strain, providing a plurality of primers complementary to regions of selected and non-selected strain, exposing to at least one probe that is complementary to non-selected strain in between primers and said probe is nucleic acid analog, amplifying by PCR and detecting the amplified product (see whole document, especially abstract, col. 2, lines 4-55 & col. 1, line 40-42). Steinmen et al teach a probe greater than 8 nucleotides (see Table 1). Steinman et al also teach separation and detection by gel electrophoresis (see col. 10, lines 4-6).

Steinmann et al differs from the instant invention in that Steinman et al do not teach PNA probe to block PCR, but relies on the teachings of Orum et al. Orum et al teach the use of PNA probes to block and selectively amplify PCR target sequences (see whole document and abstract). Orum et al teach that PNA have higher thermal stability and specificity and effectively block formation of PCR products to selectively amplify/suppress target sequences (see abstract)

Neither Steinman et al nor Orum et al teach wherein the organism is HPV or wherein the amplification is by ligase chain reaction or by rolling circle amplification. Lancaster et al teach PCR amplification of HPV (see whole document). Lancaster et al teach low risk strains HPV 6 and high risk HPV 16 (see col. 1, lines 26-27). Lancaster et al teach the association with pathogenesis of cancer (col. 1, lines 5-10). Lancaster et al teach the target regions E1, E2, L2 and L1 (see Figure 2A). Lancaster et al do not teach wherein the amplification is by ligase chain reaction or by rolling circle amplification.

Bauer et al teach a method similar to that of Lancaster et al for detecting HPV by PCR amplification (whole document and abstract). Bauer et al teach that although PCR is the preferred amplification method, amplification of target sequence in a sample may be accomplished by any know method, such as ligase chain reaction or transcription based amplification system or self-sustained sequence replication (col. 6, lines 15-40). Bauer et al teach each of the different amplification methods provides sufficient amplification so that the target sequence can be detected via sequence-specific hybridization methods (col. 6, lines 15-40).

Therefore, in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have been motivated to apply Orums et al's PNA probes to Steinman et al's method of differentiating strains in order to selectively amplify target sequences with increase stability and specificity as suggested by Orum et al. One of ordinary skill in the art at the time of the claimed invention would have been motivated to apply Lancaster et al's primers to the PCR method of Steinman and Orum et al in order to detect different strains of HPV. Lancaster et al teach that HPV infection has high correlation with cervical cancer. Thus, it would have been *prima facie* obvious to combine the PCR method of strain differentiation as taught by Steinman et al in view of Orum et al with the primers taught by Lancaster et al in order to detect the high risk strains of HPV in patients and ultimately provide diagnosis of cervical cancer. Finally, one of ordinary skill in the art at the time of the claimed invention would have been motivated to modify the HPV PCR detection method of Steinman et al and Orum et al and Lancaster et al to encompass other forms of amplification, such as ligase chain amplification based on the teaching of Bauer et al that amplification of target sequences of HPV in a sample may be accomplished by any know method including ligase chain reaction. It would be obvious to one of ordinary skill in the art that other methods such as ligase chain reaction are capable of amplifying and detecting target sequences of HPV with a reasonable expectation of success based on Bauer et al's teaching that such amplification methods provides sufficient amplification so that the target sequence can be detected via sequence-specific hybridization methods. With Respect to claim 74, Steinman et al and Orum in view of Lancaster and further in view of Bauer et al teach the method of detecting whether at least one selected strain of HPV is present in a sample as previously discussed above. Bauer et al teach a probe comprising PNA having a

sequence comprising SEQ ID NO: 6 (see SEQ ID NO: 21) with 100% identity as noted below (see alignment below).

Regarding claims 53 and 81, Lancaster et al teach the method of claim 50 and 74, wherein the probe is a hybrid comprising a nucleic acid other than PNA (col. 8, lines 46-54). Orum et al teach hybrid comprising nucleic acids other than PNA (page 5333, col. 1, third full paragraph).

Regarding claim 54, Steinman et al teach the method of claim 50, wherein at least one of said probe comprises at least 8 bases (Table I).

Regarding claims 57 and 84, Bauer et al teach the method of claims 50 and 74, wherein the conditions comprises conduction a ligase chain reaction (col. 6, lines 15-40).

Regarding claims 59 and 60, Lancaster et al teach the method of claim 50, wherein the target region for the primers of interested in regions of the HPV genome selected from E1, E2, L2 and l1 (see Figure 2A).

Regarding claim 61, Bauer et al teach the method of claim 59, wherein said region of the HPV genome is E6 (col. 7, lines 64-67).

Regarding claim 62-65 and 86-89, Lancaster et al teach the method of claim 50 and 74, wherein said at least one non-selected strain comprises a plurality of low-risk HPV strains encompassing HPV strains 6 and wherein at least one selected strain comprises a plurality of high risk HPV strains encompassing HPV strain 16 (see col. 1, lines 26 and 27). Bauer et al also teaches the low risk strain HPV 6 and the high risk strain HPV 16 (col. 6, lines 61-66).

Regarding claim 67-68 and 91, Bauer et al teach the method of claim 50 and 67, wherein at least one of the probe comprises a sequence having 100% identity to the sequence of SEQ ID NO: 6 (see col. 70, SEQ ID NO: 21). Note the following alignment:

Application SEQ ID NO: 6 - AGATACCACACGCAG

Bauer's SEQ ID NO: 21 - CTGTGGTAGATACCACACGCAGTAC

Regarding claim 70 and 93, Lancaster et al teach the method of claims 50 or 74, wherein said sample is a cervical scraping (col. 1-2).

Regarding claims 71 and 94, Steinman et al teach the method of claims 50 and 74, wherein detecting comprises in-gel electrophoresis and staining with ethidium bromide (col. 10, lines 4-7).

Regarding claim 72 and 95, Lancaster et al teach the method of claim 50 and 74, wherein a plurality of probes are provided, wherein each of said plurality is sufficiently complementary to a portion of the nucleic acid from a DNA fragment mixture or different HPV subtypes (col. 8, lines 35-45).

Regarding claims 73 and 96, Steinman et al teach the method of claims 50 and 74, wherein at least one of said at least one probe is substantially complementary to a portion of nucleic acid that is adjacent to the region of nucleic acid to which at least one of said at least one primer is substantially complementary (col. 3, lines 19-25).

Regarding claim 76, Bauer et al teach the method of claim 50 or claim 74, further comprising capturing the target selected strain onto a solid support (col. 9, lines 22-39).

6. Claims 58, 78 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Steinman et al and Orum et al in view of Lancaster et al in view of Bauer et al as previously described above and further in view of Stefano et al (US 6,287,772 B1, effective filing date April 1998). Regarding claim 58, 78 and 85, Steinman et al and Orum et al in view of Lancaster et al in view of Bauer et al teach a method for identifying or detecting whether at least one selected strain of HPV is presented in a sample as previously described above. The references teach wherein the method encompasses PCR or ligase chain reaction. None of the references teach wherein the method for detecting selected strains of HPV encompasses rolling circle amplification reactions or molecular beacon probes. However Bauer et al teach that any amplification-based assay can be utilized in the detection and analysis of HPV.

In a general teaching, Stefano et al discloses methods and compositions for detecting and quantitating target nucleic acid sequences, wherein said target nucleic acid sequences can be specific for a pathogen or a microorganism and can be from a virus, bacterium, parasite fungus or yeast (col. 11, lines 47-50). Stefano et al teaches wherein the target nucleic acid sequences can be analyzed by amplification reactions such as PCR, ligase chain reaction or rolling circle amplification (col. 11, lines 65-67 to col. 12, lines 1-4) or wherein the target nucleic acid sequences can be analyzed by molecular beacon using molecular beacon probes (col. 12, lines 4652). Based on general teachings known in the art would have been obvious to one of ordinary skill in the art at the time of the claimed invention that other forms of amplification and probes can be utilized in the HPV detection method. It would have been obvious to one of ordinary skill in the art based on the teaching of Bauer et al that any amplification-based assay can be used to analyze HPV and by the teaching of Stefano et al wherein target organism including

pathogenic viruses are amplified by rolling circle amplification. One of ordinary skill in the art would have been motivated to modify the method taught by Steinman et al and others to encompass molecular beacon probes rather than the standard probes used in the references cited therein for other means of signal detection with high specificity and disclosed by Stefano et al and known in the art.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 50-54, 57-65, 67-68, 70-74, 76-89, 91 and 93-96 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/323,188. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F. 2d 887, 225 USPQ 645 (fed. Cir. 1985).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims 17, 19, 20-30, 33, 35-37 are drawn to a method broader in scope than the claims of the instant invention and recite a method for detecting the presence of a target nucleic acid of a human papilloma virus in a sample cell, comprising the steps of suspending a sample cell in a solution, isolating a target nucleic acid of an HPV from sample cells; contacting said target nucleic acid with at least one probe comprising PNA, said at least one probe being substantially complementary to portions of nucleic acids of multiple HPV types and detecting hybridization between said at least one probe and said target nucleic acid. The claims further recite wherein the types of HPV are high risk strains of HPV and wherein analysis involves conducting PCR and capturing the target nucleic acid onto a solid support through PNA-DNA interaction. Thus, the claims of the instant invention falls entirely within the scope of the claims 17, 19, 20-30, 33, 35-37 of application 10/323,188. As the court stated in *In re Goodman*, 29 USPQ2d 2010 (CAFC 1993), "a second application-- "containing a broader claim, more generical in its character than the specific claim in the prior patent"--typically cannot support an independent valid patent". Miller, 151, U.S. at 198; See Stanley, 214 F.2d at 153. Thus, the generic invention, as noted above is "anticipated" by the species of the patented invention. Cf., Titanium metal corp. v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985) (holding that an earlier species disclosure in the prior art defeats any generic claims). This court's predecessor has held that, without a terminal disclaimer, the species claims preclude issuance of the generical application. "*In re Van Ornum*, 686 F.2d 937, 944, 214 USPQ 761, 767 (CCPA 1982); Schneller, 397 F.2d at 354".

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. No claims are allowed. However, claim 77 has not been rejected under prior art because no prior art was found wherein Alu oligonucleotides were utilized on a solid support to capture strains of a selected organism. No motivation could be found in the art for this limitation. The closest prior art not relied upon: Zietkiewicz et al (PNAS, vol. 89, pages 8448-8451, 1992) teach Alu oligonucleotide-directed PCR wherein Alu oligonucleotides are utilized as DNA markers in linkage analysis or genetic mapping studies.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

CYNTHIA WILDER
PATENT EXAMINER
7/23/05